

Kaveri et al. 10/031,938

Support for new claim 117 is found on page 7, line 12 and on page 6, line 17 of the specification as originally filed. Support for new claim 128 in the description as originally filed is to be found on p. 10, lines 7-8 ("*diseases of thrombotic nature*"), and also on page 9, line 27 ("*such as thrombosis in particular*"). Support in the description as originally filed is to be found on page 7, line 12 to page 9, line 23. Support for new claims 141-143 in the application as originally filed is found in original claim 17 and claims dependent thereon. Support for new claims 144-150 in the application as originally filed for this new claim is found in original claim 26. Support for new claims 151-154 in the application as originally filed is found on page 3, line 4 and also on page 5, line 7, and in Example I (page 16, line 25 *et seq.*), and page 19, line 20 *et seq., inter alia*.

It is submitted that no new matter is presented in the claims presented herewith. In view of the foregoing amendments and remarks, Applicants respectfully request favorable consideration and allowance of the present application.

Respectfully submitted,



Timothy J. Keefer

Attorney for Applicants

Reg. No. 35567

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WILDMAN, HARROLD, ALLEN & DIXON
225 West Wacker Drive
Chicago, Illinois 60606-1229
Telephone: (312) 201-2834
Facsimile: (312) 201-2327
e-mail: keefer@wildmanharrold.com

**ATTACHMENT TO AMENDMENT OF SERIAL NO. 10/031,938
CONTAINING MARKED-UP CHANGES TO SPECIFICATION**

On page 6, lines 17-32, continuing through to page 7, lines 1-10, please delete the existing paragraph and replace it with the following paragraph:

Hence, according to a third aspect, the present invention provides an anti-Factor VIII allo-antibody-catalysed Factor VIII degradation inhibitor. Advantageously, this inhibitor is characterized in that it comprises a protease inhibitor. Examples of protease inhibitors that can be used as anti-Factor VIII allo-antibody catalysed Factor VIII degradation inhibitors within the context of the present invention, without being limited thereto, are fluorophosphate-type inhibitors, such as DFP for example, or sulphonyl fluoride-type inhibitors, such as PMSF or AEBSF (4-(2-aminoethyl)benzenesulphonyl fluoride hydrochloride (notably marked by Roche Diagnostics GmbH, Mannheim, Germany, under the trademark Pefabloc®)), for example. More particularly, this inhibitor is characterized in that said inhibitor inhibits cleavage of the scissile bonds : Arg³⁷²-Ser³⁷³, located between the A1 and A2 domains, Tyr¹⁶⁸⁰-Asp¹⁶⁸¹, located on the N-terminus of the A3 domain, and the Glu¹⁷⁹⁴ – Asp¹⁷⁹⁵ located within the A3 domain of the Factor VIII molecule. More preferably still, this inhibitor is characterized in that it comprises a peptide or non-peptide analogue of the amino acid sequence:

Ser Val Ala Lys Lys His Pro ;

a peptide or non-peptide analogue of the amino acid sequence :

Asp Glu Asp Glu Asn Gln Ser ; or

a peptide or non-peptide analogue of the amino acid sequence :

Asp Gln Arg Gln Gly Ala Glu .

On page 20, please delete the existing table and replace it with the following table:

Amino acid sequence	Cleavage site
Ser Val Ala Lys Lys His Pro (SVAKKHP)	Arg ³⁷² – Ser ³⁷³ (R ³⁷² – S ³⁷³)
Asp Gln Arg Gln Gly Ala Glu (DQRQGAE)	Glu ¹⁷⁹⁴ – Asp ¹⁷⁹⁵ (E ¹⁷⁹⁴ – D ¹⁷⁹⁵)
Asp Glu Asp Glu Asn Gln [Sr] <u>Ser</u> (DEDENQS)	Tyr ¹⁶⁸⁰ – Asp ¹⁶⁸¹ (Y ¹⁶⁸⁰ – D ¹⁶⁸¹)